CASE REPORT

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A rare malignity observed in the appearance of angiomyolipoma; tubulocystic renal cell carcinoma after partial nephrectomy

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Abstract

Cystic neoplasms of the kidney are quite rare. Because they contain various differential diagnoses and their radiological features are not specific, their diagnosis is very difficult except for histopathological data. Usually, they can be confused radiologically with benign cysts of the kidney or angiomyolipoma. Radical or partial nephrectomy is the most commonly preferred curative treatment method when it shows features like rapidly growing or malignancy. Histopathological examination is required for definitive diagnosis. In this article, we aimed to present a rare case of tubulocystic renal cell carcinoma after partial nephrectomy in our clinic, who was followed up in another center for years with the pre-diagnosis of angiomyolipoma, in the light of the literature.

Keywords: Renal Cell Carcinoma, Angiomyolipoma, Tubulocystic Renal Cell Carcinoma

INTRODUCTION

Cystic neoplasms of the kidney, which comprise diagnostic challenges as they include various differential diagnoses and lack of specific radiological features, that represent approximately 10% of renal cell carcinomas (RCC), are rare (1). These neoplasms are followed up until their size increases since they are usually reported as benign cysts or angiomyolipomas in radiological imaging techniques such as tomography and ultrasonography. Radical or partial nephrectomy is usually a preferred surgical treatment method when these neoplasms become symptomatic that generally emerge with a flank pain or a palpable mass in the abdomen. In this article, we aimed to present a case whose histopathology was reported as tubulocystic renal cell carcinoma after partial nephrectomy performed in our clinic due to the enlargement and pain of the mass over time, followed up for years with the diagnosis of angiomyolipoma in another center.

CASE

A 53-year-old male patient first applied to an external center in 2011 due to left flank pain. Urinary system ultrasonography (USG) showed a 25×20 mm renal mass compatible with angiomyolipoma in the lower pole of the left kidney. Upon the finding, a contrast enhanced computed tomography (CT) of the abdomen was performed and the mass was interpreted as a 25×20 mm simple cortical cyst in the lower pole of the left kidney. The patient was followed up every 6 months with the diagnosis of angiomyolipoma with increased fat density. In these follow-ups, the mass had limited growth up to 35×40 mm in size. The patient applied to our clinic in 2019 with the complaint of progressive left flank pain. We performed an USG

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which indicated an exophytic 40×42 mm angiomyolipoma-compatible cystic mass in the lower pole of the left kidney. Dynamic contrast-enhanced CT was performed because the cystic mass had reached twice the size of the first measures during follow-up, and an endophytic, interpolar that located in the lower pole, Bosniak type III renal cyst was noticed in the abovementioned kidney (Figure 1). Due to the clinical condition of the patient and the high risk of malignancy of the cystic mass, this situation was explained to the patient in detail and open partial nephrectomy was planned for the patient.

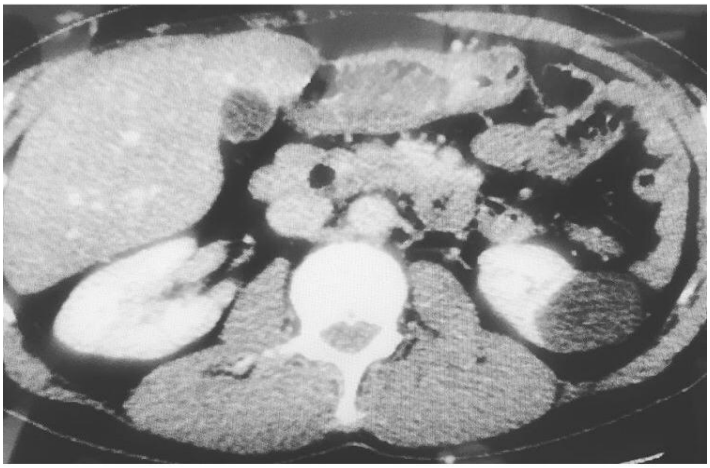

Figure 1. Pre-operative contrast-enhanced CT image of the patient (indicated by the arrow)

Pathological Diagnosis and Histochemistry

The patient underwent open left partial nephrectomy. Partial nephrectomy material examining histopathologically; 4×4×4.5 cm in size, with a macroscopically observable parenchymal surgical margin (Figure 2). Clustered smooth-walled cysts accompanied by few smooth areas recognised during analysis macroscopically. In the course of histological examination, the tumoral tissue demonstrated enlarged tubules occured with limited proliferation and cystic formation. Each cysts contained papillary structures and crusty, flat, cubic shaped cells covered the tubules and wall of the cysts as a single layer partition. In the incision made, at a distance of 0.2 cm closest to the surgical margin, nodular lesions with a thin fibrous capsular appearance, 4.6×4×4 cm in size, gray-white cross-sectional surface, and numerous cystic areas, the largest of which was 0.6 cm in diameter, were observed. It was noticed that the cysts were often single layered, sometimes multi-layered, appearing with eosinophilic cytoplasm in fluctuative amounts. and lined with a cuboidal, squamous or hobnail-like single-layered epithelium (Figure 3). An immunohistochemical analysis was obtained to affirm the diagnosis. Tumor cells were found to be CK7 and HMWCK focal positive, while AMACR and Vimentin were diffusely positive. Although there was no loss of fumarate hydratase in the tissues, S100 and CD117 were typically negative and CD10 positive. However, mutational and molecular genetic parameters could not be studied due to the lack of necessary kits in our pathology department at that time. Based on these histopathological findings, the mass resected from the lower pole of the left kidney was diagnosed as "Tubulocystic Renal Cell Carcinoma". The patient has been followed for two years without any evidence of local recurrence or distant metastasis.

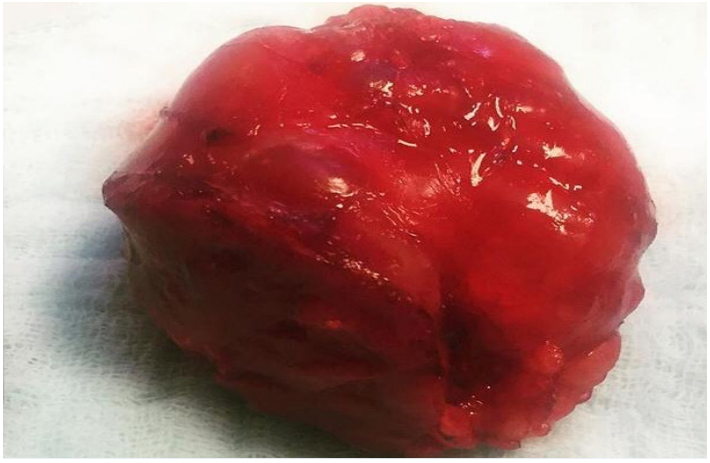

Figure 2. Partial nephrectomy material, macroscopic view.

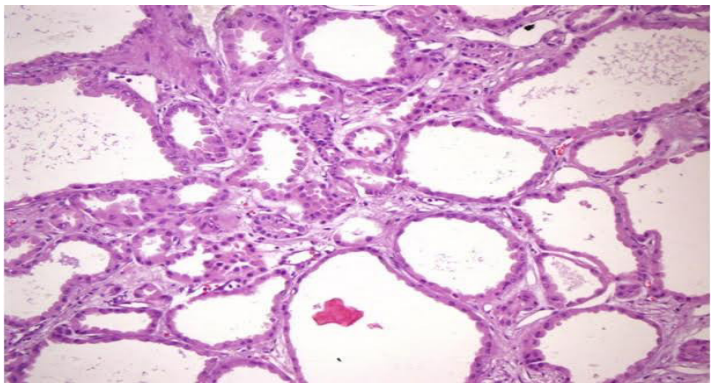

Figure 3. Tubulocystic renal cell carcinoma microscopic image (40x).

DISCUSSION

TC-RCC is defined as an uncommon kidney cancer with a tendency to behave less aggressively when compared to other urologic malignancies. Although most of these tumors enlarge slowly, they rarely progress, recur or metastasize. In clinical practice, frequently, with a male predominance (male:female ratio 7:1) and almost 60% of occurrence in the left kidney, these tumors reported more or less by the fifth or sixth decade of individuals presence (2). Although infrequent, important clinical findings such as abdominal pain, abdominal distension and hematuria might be encountered, patients are usually asymptomatic (3,4). The sizes of TC-RCCs are generally

small at the time of presentation, and approximately 40% of reported cases are less than 2 cm (5). However, patients with larger tumors or metastatic masses might experience complaints of abdominal pain, abdominal feel of distention come along with hematuria (6). The differential diagnosis of TC-RCC is likely vary and mostly includes tumors such as multilocular cystic RCC, cystic nephroma, mixed epithelial and stromal tumors, cystic oncocytoma, angiomyolipoma, and cystic form of RCC (6,7). Our patient was also followed up with the diagnosis of angiomyolipoma for years and the mass showed slow growth over time and radiological findings in subsequent examinations was reported as compatible with Bosniak type III renal cyst. Bosniak category type III-IV renal cysts are lesions with progressive malignancy rates, and hence a surgical resection is usually recommended as the main treatment method (8). Likewise, the recommended curative treatment for TC-RCC is radical nephrectomy, and the surgical procedure can be performed with an open or laparoscopic approach. However, partial nephrectomy can be performed for small tumors located superficially or peripherally. In our case, the tumor was located in the lower pole with a suitable size and location for partial nephrectomy that we performed accordingly.

Renal Cystic neoplasms comprise a few types of entities, including those newly described. A proper analysis of immunohistochemical markers is a necessity to obtain an accurate diagnosis (5). Since the biological behavior of cystic neoplasms in newly diagnosed patients is still uncertain, these patients should be monitored closely and the results should be reported properly. Considering the mild but certain risk of metastasis, all cases diagnosed with TC-RCC should be precisely followed up (5). The CT findings of TC-RCC indicate a solid mass with a thickened septum shaped as multiloculated neoplasia considered as Bosniak type II, IIF, III, or IV cysts. Moreover, considering the Bosniak classification system, MRI is more advantageous to accurately determine and categorize the cystic mass (2,9).

Cystic genre of TC-RCC challenge clinicians to distinguish it from alternate cystic masses that are considered benign such as simple renal cyst, MDK (multicystic dysplastic kidney), renal abscess, and malignant tumors, including complex renal cyst, multilocular cystic RCC, adult cystic nephroma, even MEST (mixed epithelial and stromal tumor). Simple renal cysts, particularly in the form of a complex structure, carry some radiological features identical to thin, non-contrast-enhancing inner septa accompanied by wall calcifications and lack of wall nodules that complicate the differential diagnosis. MDK, on the other hand, is characterized by multiple cysts of assorted extent unbonded with each other covering the renal parenchyma and shows minimal or no contrast enhancement. Multilocular cystic RCC is composed of multiple cysts with clear cytoplasm and lined with septal epithelial cells of fibrous tissue.

TC-RCC is observed as a well confined tumor that is non-encapsulated on macroscopic pathological examination; It is white or gray in color, Swiss cheese-like or wrapped balloon-like aspect due to spongy cysts of dissimilar extents. In Histological examination, it contains cysts of various sizes as well as tubules coated by a sole layer of hobnail, cubic cells. In some cases, it also includes cylindrical and columnar neoplastic cells specifically with eosinophilic cytoplasm. Evident nucleoli appear with a round nuclei (2). In Immunohistochemical scanning, protein expression can be demonstrated by neoplastic cells in both proximal tubules (CD10, P504S and CA-IX) and distal tubules and collecting ducts (CK7, CK19, keratin 903 and parvalbumin) in a weak and focal staining pattern of CK7. In the immunohistochemical examination of our case, the tumor cells were CK7 and HMWCK focal positive, while AMACR and Vimentin were diffusely positive. TC-RCC, previously called “Bellinian epithelioma” particularly. Besides, owing features of proximal and distal nephron differentiation and because of its morphological similarity, it was also named as “low-grade collecting ductal carcinoma”. Consequently, TC-RCC and collecting duct carcinoma, having evident histopathological diagnosis, are distinct from other neoplasms in regard to gene expression, clinical results and in the basis of immunohistochemistry.

Recent studies reveal similarities between TC-RCC and type 2 papillary RCC regarding morphological and immunohistochemically (10). Besides, both neoplasms can occasionally be encountered in the very identical lesion. Papillary form of RCC is considered to have a more aggressive course. Hence the association between papillary RCC and TC-RCC, radical nephrectomy is mainly suggested treatment method. Partial nephrectomy could be considered as an alternative option for suitable tumors. In our case, we also performed a partial nephrectomy because of the small size mass that is located in the lower pole of the polar pole.

Although a few case reports showed an inadequate response to Sunitinib (tyrosine kinase inhibitor) and Everolimus (mTOR inhibitor), Targeted therapy in Metastatic TC-RCC have not been reliably documented yet (2,11). In addition, liver and bone metastases were defined in a TC-RCC case presented by Salvatori et al., and Pazopanib and Nivolumab were administered for treatment (12). In our case, we did not consider counseling oncology, as no evidence of recurrence or metastasis was observed in the patient, whom we followed up regularly for about two years after surgery.

The biological behavior of these tumors is still not well known. Most of the tumors represent variable behavior, besides metastases to lymph nodes, liver, bone and brain have been described as well as local recurrences (13,14). Our patient was followed up for years considering it as a simple renal cyst with a benign course, afterwards surgery was required due to emerging growth in size and pain. No findings of recurrence or metastasis were detected for two-year follow-up after treatment. Some small masses reported as cysts or angiolipomas on radiological imaging should be followed closely and treated when these masses grow rapidly. TC-RCC, which can be seen rarely, should also be considered in the differential diagnosis.

CONCLUSION

TC-RCCs are tumors that predominate in males and, when examined in experienced centers, comprise remarkable distinctive features like bubble wrap aspect in macroscopy, and cysts detached by a thin fibrotic stroma that is covered by hobnail cells in microscopic appearance. However, TC-RCCs represent as cystic renal masses like Bosniak type II-IV cysts and are difficult to distinguish from other renal cystic tumors by using conventional imaging methods. Such renal cysts should undergo particular ultrasonographic examination, and lesions with these imaging features should be highlighted and noted by the radiologist to encourage earlier intervention. In order to determine the prognosis, select the appropriate treatment, and better understand the biology of these rare tumors, we believe that larger series of cases with long-term follow-up are necessary.

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Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Ethical Declaration

Informed consent was obtained from the participant and Helsinki Declaration rules were followed to conduct this study.

Author Contrubitions

Concept: BK, Design: EÖ Supervising: EÖ, Financing and equipment: EÖ, Data collection and entry: EÖ, Analysis and interpretation: EÖ, Literature search: EÖ, Writing: EÖ, Critical review: BK

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